

REMARKS

This amendment is being filed in response to the final Office Action dated April 14, 2009 (hereinafter "the Office Action"). All objections and rejections are respectfully traversed.

Applicants have amended claims 12-16 and 18-21 to better claim the invention. No new matter has been added and no new issues are raised by this amendment.

Now pending in the application are claims 1-50. Claims 37-50 were withdrawn from further consideration in response to the Examiner's restriction requirement dated June 30, 2006. Amongst claims 1-36, claims 1, 12, 22 and 28 are independent.

Applicants thank the Examiner for considering the Information Disclosure Statement (IDS) filed on March 25, 2009, accepting the petition to correct inventorship filed on March 11, 2009, and withdrawing the objection to claim 12 (Office Action at pages 2-3).

I. Summary of Rejections

In the Office Action:

claims 12-21 were rejected under 35 U.S.C. §101 as being directed to non-statutory subject matter;

claims 1, 12-19, 21, 24, 28 and 31 were rejected under 35 U.S.C. §103(a) as being obvious over U.S. Patent No. 6,882,940 to Potts, *et al.* (hereinafter "Potts") in view of a reference cited only as "Fox" in the Office Action. The Examiner indicates that the reference is from an IDS filed on "11/8/2004." Applicants believe that the Examiner meant International Patent Application No. PCT/US02/35018 to Jeffery G. Fox, cited in the November 4, 2004 IDS; and

claims 1-30 and 32-36 were rejected under 35 U.S.C. §103(a) as being unpatentable over "Mathematical Simulation and Analysis of Cellular Metabolism and Regulation" by I. Goryanin, *et al.*, Bioinformatics, 1999, Vol. 15, No. 9, pp.749-758 (hereinafter "Goryanin") in view of "Tissue Microarray (TMA) Technology: Miniaturized Pathology Archives for High-throughput *in situ* Studies" by L. Bubendorf, *et al.*, Journal of Pathology, 2001, Vol. 195, pp.72-79 (hereinafter "Bubendorf").

These rejections will be discussed separately below.

II. Application Data Sheet

The Examiner objects to the Application Data Sheet (ADS) filed on March 11, 2009, because it is not titled "Supplemental Application Data Sheet." Applicants submit a corrected Supplemental ADS herewith.

III. Claim Rejections under 35 U.S.C. §101

The Examiner rejected claims 12-21 under 35 U.S.C. §101. The Examiner has helpfully suggested that the §101 rejection could be overcome by reciting the "use of a machine within the steps of the claimed subject matter" (Office Action at page 3). In order to expedite prosecution, Applicants have amended independent claim 12 and dependent claims 13-16 and 18-21 to include "using a computer." Claims 13-21 depend from claim 12. Accordingly, Applicants respectfully urge that the pending claims are tied to a particular machine or apparatus, and therefore recite patentable subject matter under §101. Applicants respectfully urge that the Examiner reconsider and withdraw the 35 U.S.C. §101 rejection of claims 12-21.

IV. Claim Rejections under 35 U.S.C. §103(a) in view of Potts and Fox

In the Office Action, the Examiner rejected claims 1, 12-19, 21, 24, 28 and 31 under 35 U.S.C. §103(a) as being obvious over Potts in view of Fox (*See* the Office Action, page 5). Applicants respectfully traverse this rejection.

A. Claim 1

Claim 1 recites:

1. A computer-readable medium holding instructions executable in a computing device, the medium comprising one or more instructions for:
generating a result from executing a block diagram model of a biological process with a simulation engine;
gathering data directly from an in situ experimental device on which an ongoing in situ experiment of the biological process is conducted;

comparing the generated result to the data gathered from the experimental device with an analysis environment that is in communication with the simulation engine; and
modifying the model of the biological process based on the comparison to correct the model of the biological process.

Applicants respectfully urge that Potts and Fox, alone or in any reasonable combination, do not disclose or suggest at least the following features of claim 1: *generating a result from executing a block diagram model of a biological process with a simulation engine*; and *modifying the model of the biological process based on the comparison to correct the model of the biological process.*

With regards to *generating a result from executing a block diagram model of a biological process with a simulation engine*, the Examiner recognizes that Potts does not teach a block diagram (Office Action at page 6). Potts fails to disclose executing a block diagram model of a biological process. Instead, the Examiner relies on Fox for a block diagram model of a biological process, arguing that it would have been obvious to combine Fox's block diagram with Potts' prediction algorithm. However, Fox also does not disclose or suggest a block diagram model of a biological process.

Applicants can find no reference in Fox to a block diagram model of a biological process. Like Potts, Fox describes a "network" model of a process. In Potts, the network is a neural network (Potts at col. 24, §2.8). The Examiner asserts that Fox describes a block diagram model of a biological process at claims 9 and 11, and Figures 7 and 8 (Office Action at page 6). Fox's claim 9 recites:

A computer system for use in inferring a network model of a process, comprising computer instructions for: generating a search space of candidate networks; reducing said search space by eliminating one or more non-fitting candidate networks to form a reduced search space; testing said candidate networks in said reduced search space against one or more criteria to identify an ensemble of networks; and modeling said process using said ensemble of networks.

and Fox's claim 11 recites:

The computer system of Claim 9, wherein said process is a biologic process.

The claims from Fox recite “a network model of a process,” and not a ***block diagram model of a biological process***. A network model of a process is not a block diagram model of a biological process.

Figures 7 and 8 of Fox also do not disclose or suggest a block diagram model of a biological network. Figure 7 of Fox “is flowchart of a network inference process.” The biological process used in the steps shown in Figure 7 is described as a “network of links” (see, e.g., steps 710 and 750). This is consistent with the network model of a process described in the rest of Fox, which is not a block diagram model of a biological process. Figure 8 of Fox “depicts schematically one process for inferring a biological network.” In Figure 8, the biological process is also described as a “network” (see, e.g., element 14). Nowhere in Fox is there a depiction or a description of a biological process modeled as a block diagram model.

Based on the Examiner’s comments at page 9 of the Office Action (with respect to the Goryanin and Bubendorf references), it appears that the Examiner is interpreting the diagrams depicted in Figures 7 and 8 (e.g., a flowchart in Figure 7 and a schematic depiction of the software modules in Figure 8), as “block diagrams.” However, Applicants respectfully urge that the diagrams in Figures 7 and 8 in Goryanin and Bubendorf are not ***a block diagram model of a biological process***. Figure 7 is a flowchart depicting steps performed in an algorithm. The steps reference a network model of a biological process, but the diagram depicted is a diagram of the algorithm, not the biological process. Likewise, in Figure 8, software components are depicted, not a biological process.

With regards to ***comparing the generated result to the data gathered from the experimental device***, Potts and Fox fail to disclose or suggest this claimed feature as well. In the Office Action, the Examiner alleges that comparing skin conductance with a threshold value, described in Potts in claims 1 and 25, and correlating blood glucose measurements with “out of sample” predictions, described in Potts at column 8, lines 45-67, teaches the Applicants’ claimed ***comparing the generated result to the data gathered from the experimental device***. Applicants respectfully disagree.

Nowhere does Potts disclose or suggest that a result generated from executing a block diagram model of a biological process is compared to the data gathered from the experimental

device. There is no disclosure in Potts of comparing a result generated from executing a block diagram model of a biological process with a certain value. As noted above, Fox also does not disclose or suggest a block diagram model of a biological process. Therefore, Potts and Fox, alone or in any reasonable combination, do not disclose or suggest Applicants' claimed *comparing the generated result to the data gathered from the experimental device*.

With regards to *modifying the model of the biological process based on the comparison to correct the model of the biological process*, Potts and Fox, alone or in any reasonable combination, fail to disclose this feature of Applicants' claim 1. In the Office Action, the Examiner alleges that Potts discloses "training" a prediction algorithm and that this disclosure teaches Applicants' claimed *modifying the model of the biological process based on the comparison to correct the model of the biological process*. Applicants respectfully disagree.

Nowhere does Potts disclose or suggest modifying a block diagram model of a biological process. In Potts, the prediction algorithm is an algorithm that is used to predict the GlucoWatch biographer system values. See Potts, columns 23-27. The prediction algorithm described in Potts is not a block diagram model of a biological process. As noted above, Fox also does not disclose or suggest a block diagram model of a biological process. Therefore, Potts and Fox, alone or in any reasonable combination, do not disclose or suggest Applicants' claimed *modifying the model of the biological process based on the comparison to correct the model of the biological process*.

For at least the reasons set forth above, Applicants respectfully urge that Potts and Fox, alone or in any reasonable combination, do not disclose or suggest Applicants' claim 1. Therefore, Applicants respectfully request that the above 35 U.S.C. §103(a) rejection of claim 1 be withdrawn.

B. Claim 12

Claim 12 recites:

12. A method for modifying a model of a biological process, the method comprising:
 - accessing a block diagram model of the biological process;
 - generating a result from an execution of the model of the biological process;*

gathering data directly from an in situ experimental device on which an ongoing in situ experiment is conducted;
comparing the generated result to the data gathered from the ongoing in situ experiment; and
modifying the model of the biological process based on the comparison to correct the model of the biological process.

As discussed above with respect to claim 1, Potts and Fox, alone or in any reasonable combination, fail to disclose or suggest *generating a result from an execution of the model of the biological process*; *comparing the generated result to the data gathered from the experimental device*; and *modifying the model of the biological process based on the comparison to correct the model of the biological process*. These features are also present in claim 12. Thus, Potts and Fox, alone or in any reasonable combination, do not disclose or suggest all of the features of Applicants' claim 12. Therefore, Applicants respectfully request that the above 35 U.S.C. §103(a) rejection of claim 12 be withdrawn.

C. Claims 13-19 and 21

Claims 13-19 and 21 depend on claim 12 and, as such, incorporate all of the features of claim 12. For at least the reasons set forth above with respect to claim 12, Applicants respectfully urge that Potts and Fox, alone or in any reasonable combination, fail to disclose or suggest all of the features of claims 13-19, and 21. Therefore, Applicants respectfully request withdrawal of the above 35 U.S.C. §103(a) rejection of claims 13-19 and 21.

D. Claim 24

As discussed above with respect to claim 1, Potts and Fox, alone or in any reasonable combination, fail to disclose or suggest *generating a result from an execution of the model of the biological process*; *comparing the generated result to the data gathered from the experimental device*; and *modifying the model of the biological process based on the comparison to correct the model of the biological process*. These features are also present in claim 22. Claim 24 depends on claim 22 and, as such, incorporates all of the features of claim 22. Thus, Potts and Fox, alone or in any reasonable combination, do not disclose or suggest all of the features of Applicants' claim 24. Therefore, Applicants respectfully request that the above 35 U.S.C. §103(a) rejection of claim 24 be withdrawn.

E. Claim 28

Claim 28 recites:

28. A computer-readable medium holding instructions executable in a computing device, the instructions comprising one or more instructions for:
generating a result from executing a block diagram model of a biological process;
gathering data directly from an in situ experimental device on which an ongoing in situ experiment of the biological process is conducted;
comparing the result to the data gathered from the experimental device; and
modifying the model of the biological process based on the comparison.

As discussed above with respect to claim 1, Potts and Fox, alone or in any reasonable combination, fail to disclose or suggest *generating a result from executing a block diagram model of a biological process, comparing the generated result to the data gathered from the experimental device, and modifying the model of the biological process based on the comparison to correct the model of the biological process*. These features are also present in claim 28. Thus, Potts and Fox, alone or in any reasonable combination, do not disclose or suggest all of the features of Applicants' claim 28. Therefore, Applicants respectfully request that the above 35 U.S.C. §103(a) rejection of claim 28 be withdrawn.

F. Claim 31

Claim 31 depends on claim 28 and, as such, incorporates all of the features of claim 28. For at least the reasons set forth above with respect to claim 28, Applicants urge that Potts and Fox, alone or in any reasonable combination, fail to disclose all of the features of claim 31. Therefore, Applicants respectfully request withdrawal of the above 35 U.S.C. §103(a) rejection of claims 31.

V. Claim Rejections under 35 U.S.C. §103(a) in view of Goryanin and Bubendorf

In the Office Action, the Examiner rejected claims 1-30, 32-36 and 51 under 35 U.S.C. §103(a) as being unpatentable over Goryanin in view of Bubendorf (*See the Office Action, pages 7-9*). Applicants respectfully traverse this rejection.

A. **Claim 1**

Applicants respectfully urge that Goryanin and Bubendorf, taken either alone or in any reasonable combination, do not disclose or suggest at least the following features of claim 1: ***generating a result from executing a block diagram model of a biological process with a simulation engine and gathering data directly from an in situ experimental device on which an ongoing in situ experiment of the biological process is conducted.***

With regards to ***generating a result from executing a block diagram model of a biological process with a simulation engine***, Goryanin in combination with Bubendorf fails to disclose or suggest executing a block diagram model of a biological process.

In the Office Action, the Examiner asserts that “Goryanin shows a block diagram describing all the system components and programs required for generating results.” However, as discussed above with reference to the rejection of claim 1 in view of Potts and Fox, a diagram that shows system components or software modules is not ***a block diagram model of a biological process***. Therefore, Goryanin fails to disclose or suggest Applicants’ claimed ***generating a result from executing a block diagram model of a biological process with a simulation engine***.

Bubendorf is cited by the Examiner to provide teachings for an in situ experiment (See the Office Action, page 10). However, Bubendorf is silent about a block diagram model of a biological process. Bubendorf does not disclose or suggest Applicants’ claimed ***generating a result from executing a block diagram model of a biological process with a simulation engine***, which is present in claims 1 and 28. Although Bubendorf is combined with Goryanin, the combination does not disclose or suggest generating a result from executing a block diagram model of a biological process.

With regards to ***gathering data directly from an in situ experimental device on which an ongoing in situ experiment of the biological process is conducted***, the combination of Goryanin and Bubendorf fails to disclose or suggest this claimed feature as well.

The Examiner recognizes that Goryanin fails to disclose or suggest the above claimed feature. (See the Office Action, page 8).

The Examiner also recognizes that Bubendorf fails to disclose or suggest an ongoing in situ experiment. (See the Office Action, page 8). The Examiner, however, asserts that “this limitation would have been obvious to one of ordinary skill in the art since they employ a computer assisted method,” and “[t]he rationale would have been to increase the number of data analyzed to improve statistical results in a clinical setting [Introduction].” (See the Office Action, page 10). Applicants respectfully disagree.

In Applicants’ claim 1, experimental data is directly gathered from an ongoing in situ experiment of a biological process so that a block diagram model of the biological process may be modified in real time. This feature is not obvious over Bubendorf, which only describes Tissue Microarray (TMA) technologies and in situ tissue analyses (See Bubendorf, Abstract). Although Bubendorf discusses the construction of a TMA for use in in situ studies, Bubendorf does not disclose or suggest Applicants’ claimed ***gathering data directly from an in situ experimental device on which an ongoing in situ experiment of the biological process is conducted***, which is present in claim 1. Bubendorf is silent about gathering data directly from an ongoing in situ experiment. Although Bubendorf is combined with Goryanin, the combination suggests, at most, that the TMA data may be entered by a user. The combination does not disclose or suggest gathering data directly from an ongoing in situ experiment.

The Examiner asserts that one having ordinary skill in the art would be motivated to modify Bubendorf to provide an “ongoing” in situ experiment because to do so would “increase the number of data analyzed to improve statistical results in a clinical setting.” However, Bubendorf explicitly notes that the described methodology provided an analysis that was “highly representative” of donor tissues (Bubendorf at Abstract). Accordingly, one having ordinary skill in the art would not be motivated to “improve the statistical results” of an analysis that is already “highly representative” of the underlying system.

For at least the reasons set forth above, Applicants respectfully urge that Goryanin and Bubendorf, taken alone or in any reasonable combination, do not disclose or suggest all of the features of Applicants’ claim 1. Therefore, Applicants respectfully request that the above 35 U.S.C. §103(a) rejection of claim 1 be withdrawn.

B. Claims 2-11

Claims 2-11 depend on claim 1 and, as such, incorporate all of the features of claim 1. For at least the reasons set forth with respect to claim 1, Applicants respectfully urge that Goryanin and Bubendorf, taken alone or in any reasonable combination, fail to disclose or suggest all of the features of claims 2-11. Therefore, Applicants respectfully request that the above 35 U.S.C. §103(a) rejection of claims 2-11 be withdrawn.

C. Claim 12

As discussed above with respect to claim 1, Goryanin and Bubendorf, taken alone or in any reasonable combination, fail to disclose or suggest *generating a result from an execution of the model of the biological process*; and *gathering data directly from an in situ experimental device on which an ongoing in situ experiment is conducted*. These features are also present in claim 12. Thus, Goryanin and Bubendorf, taken alone or in any reasonable combination, do not disclose or suggest all of the features of Applicants' claim 12. Therefore, Applicants respectfully request that the above 35 U.S.C. §103(a) rejection of claim 12 be withdrawn.

D. Claims 13-21

Claims 13-21 depend on claim 12 and, as such, incorporate all of the features of claim 12. For at least the reasons set forth above with respect to claim 12, Applicants respectfully urge that Goryanin and Bubendorf, taken alone or in any reasonable combination, fail to disclose or suggest all of the features of claims 13-21. Therefore, Applicants respectfully request withdrawal of the above 35 U.S.C. §103(a) rejection of claims 13-21.

E. Claim 22

As discussed above with respect to claim 1, Goryanin and Bubendorf, taken alone or in any reasonable combination, fail to disclose or suggest *generating a result from an execution of the model of the biological process*; and *gathering data directly from an in situ experimental device on which an ongoing in situ experiment of the biological process is conducted*. These features are also present in claim 22. Thus, Goryanin and Bubendorf, taken alone or in any reasonable combination, do not disclose or suggest all of the features of Applicants' claim 22.

Therefore, Applicants respectfully request that the above 35 U.S.C. §103(a) rejection of claim 22 be withdrawn.

F. Claims 23-27

Claims 23-27 depend on claim 22 and, as such, incorporate all of the features of claim 22. For at least the reasons set forth above with respect to claim 22, Applicants respectfully urge that Goryanin and Bubendorf, taken alone or in any reasonable combination, fail to disclose or suggest all of the features of claims 23-27. Therefore, Applicants respectfully request withdrawal of the above 35 U.S.C. §103(a) rejection of claims 23-27.

G. Claim 28

As discussed above with respect to claim 1, Goryanin and Bubendorf, taken alone or in any reasonable combination, fail to disclose or suggest *generating a result from executing a block diagram model of a biological process*, and *gathering data directly from an in situ experimental device on which an ongoing in situ experiment of the biological process is conducted*. These features are also present in claim 28. Thus, Goryanin and Bubendorf, taken alone or in any reasonable combination, do not disclose or suggest all of the features of Applicants' claim 28. Therefore, Applicants respectfully request that the above 35 U.S.C. §103(a) rejection of claim 28 be withdrawn.

H. Claims 29, 30 and 32-36

Claims 29, 30 and 32-36 depend on claim 28 and, as such, incorporate all of the features of claim 28. For at least the reasons set forth above with respect to claim 28, Applicants respectfully urge that Goryanin and Bubendorf, taken alone or in any reasonable combination, fail to disclose or suggest all of the features of claims 29, 30 and 32-36. Therefore, Applicants respectfully request withdrawal of the above 35 U.S.C. §103(a) rejection of claims 29, 30 and 32-36.

CONCLUSION

In view of the above comments, Applicants believe that the pending application is in condition for allowance and urges the Examiner to pass the claims to allowance. Should the Examiner feel that a teleconference would expedite the prosecution of this application, the Examiner is urged to contact the Applicant's attorney at (617) 227-7400.

Please charge any shortage or credit any overpayment of fees to our Deposit Account No. 12-0080, under Order No. MWS-109RCE. In the event that a petition for an extension of time is required to be submitted herewith, and the requisite petition does not accompany this response, the undersigned hereby petitions under 37 C.F.R. §1.136(a) for an extension of time for as many months as are required to render this submission timely. Any fee due is authorized to be charged to the aforementioned Deposit Account.

Dated: June 15, 2009

Respectfully submitted,

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